

Roxithromycin compared with erythromycin against genitourinary chlamydial infections

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SUMMARY The efficacy and safety of roxithromycin 300 mg once a day was compared with that of erythromycin 500 mg twice a day, both for seven days, in a double blind study of 281 patients (188 men, 93 women) with genitourinary chlamydial infections. At the end of the treatment 251 (89%) patients were evaluable, and at follow up two weeks later 227 (81%) were evaluable. The bacteriological cure rate was close to 100% at the end of both treatment regimens. At follow up 55/75 (73%) evaluable men and 38/39 (97%) evaluable women treated with roxithromycin were chlamydia negative compared with 50/71 (70%) evaluable men and 37/42 (88%) evaluable women treated with erythromycin. Of the 47 who were still chlamydia positive, reinfection could not be excluded in half the men and all the women.

Side effects were mainly gastrointestinal and were found in about 15% of patients receiving each treatment, but did not necessitate discontinuing treatment in any case. Roxithromycin seems to be as safe and efficacious as erythromycin in treating chlamydial infections in men and women, and it has the advantage that treatment is by a single daily dose.

Tetracycline and erythromycin are the drugs of choice in treating genitourinary chlamydial infections. The recommended periods of treatment and daily doses have varied in different studies from one to two weeks and from 1 g to 2 g divided into two, three, or even four daily doses.¹ Compliance of patients and thus the result of treatment depends, among other things, on the simplicity of the treatment. Roxithromycin is a new macrolide antibiotic with the same structure as erythromycin but a longer half life of about 10-12 hours, which indicates that this drug can be administered once a day. In vitro and in vivo studies have shown that roxithromycin is effective against *Chlamydia trachomatis*,^{2,3} and that it is safe, well tolerated, and well absorbed after administration by mouth.³ To evaluate this further, we compared treatment with roxithromycin 300 mg a day with erythromycin 500 mg twice a day, both for seven days, in men and women with uncomplicated genitourinary chlamydial infections.

Patients, materials, and methods

All men and women attending our outpatient venereal disease clinic are screened routinely for genitourinary chlamydial infections. We asked all patients who attended with uncomplicated chlamydial infections during a four month period to participate in the study. We excluded patients who had received antibiotics within the previous three days, who had concomitant gonococcal infection, a history of hypersensitivity to macrolide antibiotics, or severely impaired hepatic or renal function, and pregnant and nursing women.

We randomly assigned the patients to a double blind, double dummy, multiple dose trial, comparing roxithromycin 300 mg once a day with erythromycin ethylsuccinate 500 mg twice a day by mouth for seven days.

We asked the patients to return on days 8 and 21 after the start of treatment. Patients' complaints of urethral or vaginal discharge and pain were registered before entering the study and again at both follow up visits. Laboratory tests (haematology, liver and kidney function tests, and urine analysis) were performed before entering the study and again at the first follow up visit, at which time side effects were also listed.

We collected urethral and cervical samples with

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cotton tipped aluminium swabs before the patients entered the study and at both follow up visits. *C. trachomatis* was identified by using cycloheximide treated McCoy cells⁴ followed by iodine staining and estimation of inclusion counts.

Sexual partners of the patients were encouraged to attend for examination, but were not treated epidemiologically.

The results were compared statistically by the χ^2 test or Fisher's exact test.

Results

We enrolled 281 patients (188 men, 93 women) in the study. Of the men, 88% (166) were evaluable on day 8 and 78% (146) on day 21. Of the women, 91% (85) were evaluable on day 8 and 87% (81) on day 21 (table). Evaluable patients were those who had taken the complete dose of the drug, returned for the follow up visits, and had not been treated with any other medication that could interfere with the results. Of those excluded, four men and one woman had concomitant gonococcal infection that had not been diagnosed at enrolment; the rest had not attended both follow up visits. None of the patients attending follow up had stopped taking the medication because of side effects. The patients in the two treatment groups were comparable for age, sex, and initial symptoms. More men treated with erythromycin than roxithromycin were lost to follow up, but the difference was not significant, whereas similar numbers of women were lost to follow up from the two treatment groups. At the start of treatment, symptoms compatible with genitourinary chlamydial infection were present in 147 (78%) men and 47 (51%) women. Symptoms in the men included discharge and urethral smears contain-

ing more than five polymorphonuclear leucocytes per high power field ($\times 1000$ magnification).

Bacteriological efficacy

The table shows the results at both follow up visits. Immediately after treatment (day 8) bacteriological cure was seen in 100% of men (87/87) and women (40/40) treated with roxithromycin and in 99% (78/79) of men and 100% (45/45) of women treated with erythromycin.

Two weeks after the end of treatment (day 21) 73% (55/75) of the men treated with roxithromycin were chlamydia negative compared with 70% (50/71) of the men treated with erythromycin (not significant). Of the 41 men who were still chlamydia positive, half (10/20) of those who received roxithromycin and 57% (12/21) of those who received erythromycin said that reinfection was possible. The relapse rate in men might therefore have been as low as 15% in those treated with roxithromycin (10/65) or with erythromycin (9/59).

Two weeks after the end of treatment 97% (38/39) of the women treated with roxithromycin and 88% (37/42) of the women treated with erythromycin were chlamydia negative (not a significant difference). All women who were chlamydia positive at the last follow up visit had had sexual contact since the previous visit, so reinfection could not be excluded.

Roxithromycin and erythromycin thus had equal cure rates, but for both treatment regimens the cure rates were higher in women than in men, irrespective of the percentages of true relapses or reinfections.

Clinical efficacy

At the day 21 follow up visit the clinical efficacy rate in the 129 evaluable men who had had symptoms initially

Table Bacteriological response in 281 patients (188 men, 93 women) with genitourinary chlamydial infections treated with roxithromycin 300 mg daily or erythromycin 500 mg twice a day for seven days

	Day 8 follow up		Day 21 follow up	
	Roxithromycin (n = 137)	Erythromycin (n = 144)	Roxithromycin (n = 137)	Erythromycin (n = 144)
Men:				
Chlamydia negative	87	78	55	50
Chlamydia positive because of:				
Relapse	0	1	20	21
Reinfection	0	1	10	9
Not evaluable	0	0	10	12
Not evaluable	5	17	17	25
Total	92	96	92	96
Women:				
Chlamydia negative	40	45	38	37
Chlamydia positive because of:				
Relapse	0	0	1	5
Reinfection	0	0	0	0
Not evaluable	0	0	1	5
Not evaluable	5	3	6	6
Total	45	48	45	48

was 84% (57/68) in those treated with roxithromycin and 82% (50/61) in those treated with erythromycin (not significant). Those who still had symptoms were all chlamydia positive because of reinfection or relapse.

At the day 21 follow up visit the clinical efficacy rate in the 42 evaluable women who had had symptoms initially was 95% (20/21) in those treated with roxithromycin and 86% (18/21) in those treated with erythromycin (not significant). Those who still had symptoms were all chlamydia positive, and reinfection could not be excluded.

Side effects

The most common side effects were gastrointestinal complaints including abdominal pain and nausea, which were recorded in 15% (21/137) of the patients receiving roxithromycin and 16% (23/144) of those receiving erythromycin. Other minor side effects, such as tiredness, headache, and slight itching, were registered equally often in 1% to 5% of patients receiving either treatment regimen. Vaginal candidiasis was found in two women, one treated with roxithromycin and one with erythromycin. Slight erythema was seen in two patients treated with erythromycin. None of the recorded side effects necessitated discontinuation of the treatment.

Laboratory tests

Two men, who had normal results before treatment and were both treated with erythromycin, showed increased liver function test results after treatment, one had a raised total bilirubin concentration only, and one had increased serum glutamic oxaloacetic transaminase (SGOT) and lactate dehydrogenase (LDH) activities. These patients had no known history of liver disease. None of the other patients tested showed any signs of haematological, renal, or hepatic toxicity during treatment.

Discussion

The recommended optimum daily doses and periods of treatment for eradicating genitourinary chlamydial infections differ between studies of patients treated with tetracycline or erythromycin. Treatments of choice according to the Centers for Disease Control are tetracycline 500 mg four times a day for seven days or erythromycin 500 mg four times a day for seven days for patients who cannot tolerate tetracycline and for pregnant women.⁵ Several studies have, however, shown that 1 g a day of tetracycline⁶⁻⁸ or erythromycin⁶⁻¹⁰ for seven days^{6,7,9} or 14 days⁸⁻¹⁰ have had satisfactory effects. Shorter durations of treatment have not been recommended.¹¹⁻¹³

Erythromycin given in doses of 2 g a day has a high

incidence of gastrointestinal side effects that decreases compliance and makes more patients discontinue the treatment.¹⁴ There therefore seems to be a need for further studies elucidating the effect of other macrolides in genitourinary chlamydial infections. In this study we found that roxithromycin 300 mg once a day and erythromycin 500 mg twice a day, given orally for seven days, had similar effects. Gastrointestinal side effects were recorded in about 15% of the patients irrespective of the treatment, but not to a degree that caused any of the patients evaluable to discontinue the treatment. That less frequent administration of treatment is an important advantage in patient compliance has been shown in a study comparing treatment with doxycycline with tetracycline in patients with gonococcal infections.¹⁵ Roxithromycin should therefore be preferable to erythromycin when treating patients with chlamydial infections.

Some studies have found that more women than men with chlamydial infections are cured when given the same treatment,^{11,14} a difference that might be related to lower serum concentrations in patients with greater body weights.¹⁴ The same trend was also found in this study, with higher cure rates in women than men in both treatment groups. The cure rates in different studies are difficult to compare because of differences in duration of follow up and whether sexual partners are treated epidemiologically. In this study half the men and all the women still chlamydia positive when evaluated two weeks after the end of the treatment might have been reinfected, which gave a cure rate for roxithromycin of 74% to 87% in men and 97% to 100% in women. The corresponding cure rate for erythromycin was 71% to 87% in men and 88% to 100% in women. We therefore conclude that roxithromycin seems to be a safe and effective alternative treatment for genitourinary chlamydial infections, and has the advantage of being administered as a single daily dose.

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